DIET ADJUSTMENT AND INSULIN THERAPY IN DIABETES MELLITUS*

By ERNEST S. du BRAY, M. D., San Francisco
(From the Department of Medicine in the University of California Medical School.)

I. *Introduction*—In a subject of such magnitude, as expressed by the title of this paper, it will be possible to present only those principles which appear of first importance in the management of uncomplicated diabetes. In spite of the discovery of the pancreatic extract, insulin, all authorities agree that diet adjustment must remain the basis of diabetic management.

For a long time, diabetes has been generally regarded as the most inadequately treated systemic disease in medicine. This has resulted largely from the failure of some physicians to master a few fundamental principles of dietetics, without which successful treatment is impossible. However, with the introduction of insulin, it has become even more incumbent upon them to plan and control, by exact quantitative methods, the total dietary regime of the patient.

II. *Diet Adjustment*—Diet adjustment implies primarily the preparation of a diet with the proper balance of protein, fat, and carbohydrates, and at the same time with a known food value in calories, which will be sufficient to answer the wear and tear and the energy requirements of the particular individual.

The brilliant contribution of Woodyatt, in 1921, has revolutionized our method of diet adjustment. Woodyatt showed that three-fifths of the protein, one-tenth of the fat, plus the total carbohydrates of any diet, is burned in the organism as glucose. This was a radical deviation from our former ideas as to what composed the available glucose of the diet.

The second fundamental principle he advanced dealt with the relation of the amount of fatty acid in the diet, to the amount of glucose; in other words, he showed that a diet in which the total fatty acid in grams is not more than one and five-tenths times the total available glucose in grams will be found safe and advantageous in most cases. This conception he expressed by the formula: The total fat of the diet should not exceed twice the carbohydrate plus one-half the protein.

With these two fundamental principles in mind, the ratio of the three components, P, F, and C, can be readily determined and the diabetic assured of a safe or balanced diet. From the Aub-Dubois calculations, it can be estimated that an adult with average nutrition will utilize, in twenty-four hours, approximately thirty calories per kilo of body weight. This necessary fuel must be obtained from the P, F, and C in the food, or from the body tissues. One gram of C or P will yield four calories, and one gram of F, nine calories. In the animal economy, a certain amount of P is absolutely essential for growth and to replace nitrogenous waste. This amount is usually estimated to be from .7 to 1.0 gram per kilo of body weight in the adult, and a somewhat higher figure in infancy and childhood. With these figures as a basis for calculation, the proper caloric value of diets in diabetes are readily determined.

III. *Objects of Treatment*—Before proceeding further, it may be well to recall the objects of treatment in diabetes. These can be grouped under three heads:

1. The maintenance of body weight, strength, and efficiency. This I consider the prime object of treatment. Formerly this was difficult to attain by our undernutrition methods, because when the diet was increased above a certain point, the disease showed rapid progression and when it was decreased, the patient lost strength and efficiency.

2. The maintenance of a urine sugar-free and a normal blood sugar-level. This I believe is of extreme importance, and although some authorities are inclined to put less weight on these laboratory data, particularly since the advent of insulin, I feel that all experience with the management of diabetes points to the value of a urine sugar-free and the maintenance of a normal blood-sugar level.

3. The prevention of acidosis. Ketonuria has always been the danger signal in diabetes, and it goes without saying it remains the one thing above all others to prevent. Besides the abnormal metabolism of glucose, diabetes is characterized by a defective metabolism of fat. "Fats burn in the flame of the carbohydrates," and so, with a marked reduction in the burning of carbohydrates, the fat metabolism is upset. Fat is incompletely burned, with the result of an accumulation in the blood and tissues of fatty acids, such as diacetic acid and acetone. These so-called ketone bodies may be derived from the protein as well as the fat, but to a lesser degree; the former yielding in terms of fatty acid a possible 46 per cent by weight, and the latter 90 per cent. The point of all this is, that these ketogenic components of the diet must, therefore, be balanced by the anti-ketogenic glucose, which is produced not only from the carbohydrate food, but also in smaller amounts from the proteins and fats according to the first principle of Woodyatt, referred to above. This is roughly the chemical mechanism of the production of acidosis in diabetes. To discuss the entire subject of acidosis and its management, at this point, would take me too far afield. However, it will be referred to later when dealing with the use of insulin.

IV. *The Use of Insulin*—So much for diet adjustment and the objects of treatment in diabetes.

Insulin is the active principle derived from the Islands of Langerhans of the pancreas. The story of its brilliant discovery by Banting and Best at the University of Toronto needs no repetition here. The commercial product of this substance, now in use, is manufactured by the Eli Lilly Company of Indianapolis, and is called iletin. It is supplied to the profession in small glass vials in two strengths, designated as H-10 and H-20, and can be used effectively only by the subcutaneous and the intravenous routes.

In my work, all patients presenting themselves for treatment are hospitalized for a preliminary

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study, which requires from four to six weeks. The object of hospitalization is twofold: First, to determine accurately the severity of the case and establish the level of the natural glucose tolerance; and second, to educate the patient in the use of quantitative diets and the use of insulin, if it is found that this is required.

The actual procedure I have found useful for the great majority of uncomplicated cases is somewhat as follows: The first thing to be determined is the patient's natural tolerance for glucose; in other words, the amount of glucose that the individual can burn per twenty-four hours, without the artificial aid of insulin. On admission to the hospital, the patient is weighed and put to bed. The daily twenty-four-hour urine specimens are collected and tested qualitatively for the presence of sugar and ketone bodies, and the quantitative amount of glucose in the urine is also determined. A blood sample is collected each morning before breakfast to determine the fasting blood-sugar level.

The first test diet I use in most instances contains a glucose value of 100 grams, in which the relative amounts of P. F, and C are determined by the Woodyatt formulae, referred to above. For instance, in a sixty kilogram patient, the P content of this diet would be placed at 60 grams (i. e., allowing a gram of P per kilo of body weight, as is necessary for basal requirements); the F equals 130, and the C equals fifty. This diet supplies a caloric value of 1610 calories, which would be slightly under the calculated basal requirement of 1800 calories for a sixty kilogram individual. The patient is then observed on this diet for several days, and if he becomes sugar-free and the blood-sugar shows a tendency to fall to the normal level, the diet temporarily remains unchanged. If this status of conditions persists for a week or ten days, it is apparent that the patient has a natural tolerance of 100 grams of glucose or more. Additions to the diet are then cautiously made. Ten to 15 grams of both F and C are added, the protein remaining unchanged. Sooner or later, as these additions are made and the glucose value of the diet rises, the point is reached at which the urine shows sugar and the blood-sugar tends to rise. Just below this point, we may say, for practical purposes, lies the patient's natural glucose tolerance.

On the other hand, it is frequently found that the urine and blood-sugar level will not become normal on a diet containing 100 grams of glucose. In such cases, the diet is gradually reduced in its glucose value by reductions in the F and C components until the level is reached at which the urine and blood becomes normal. If the glucose tolerance is very low, i. e., anything less than 35 grams, as a rule, nothing is gained by prolonging the undernutrition period, and valuable time is lost in doing so. In such a case, it is apparent that the use of insulin is indicated to make up the difference between the low natural tolerance and a proposed diet which will be adequate for the individual, in order for him to attain the three objects of treatment, namely, to maintain bodily vigor and efficiency; to maintain a normal urine and blood, and to prevent the progression of the disease, with acidosis constantly threatening. The decision to use insulin made, it is necessary to raise the diet at once to a glucose value of 75 to 100 grams. This will protect the patient from the so-called hypoglycemic reaction caused by a subnormal blood-sugar following the administration of insulin. I shall have more to say concerning these reactions and their prevention a little later. The initial dose of insulin should be small, preferably five units, either twice or three times a day, about half an hour before meals. Following the administration of insulin, the same close observation of the urine and blood-sugar level are important. In the course of observation, the urinary sugar usually disappears before the blood-sugar level comes to normal. As the insulin dosage is raised from fifteen units a day to twenty, twenty-five, and so on, eventually the patient becomes sugar-free, and following this the blood-sugar falls slowly to normal. Again the diet is increased by 20 grams in its glucose value. With increased diet an increased insulin dosage is required. When the point is reached at which the diet is adequate and the insulin dosage sufficient to just keep the patient sugar-free and his blood-sugar normal, the balance is struck for the individual under basal conditions. It is necessary now to get the patient out of bed as soon as possible and resume his normal activity. The energy requirements of the ambulant patient are increased from 40 to 50 per cent, so the diet must be raised to meet these needs. It is frequently found that the rest in bed on a low caloric diet, plus the assistance which the insulin offers in relieving the strain on an overworked pancreas, brings about an apparent gain in natural tolerance within a few weeks. With increased tolerance, the insulin dosage must be gradually reduced.

The amount of glucose which one unit of insulin will burn varies with individual cases. In the severe cases with low tolerance it appears to be from 1 to 2 grams, whereas in the milder cases, one unit will take care of 3 to 4 grams of glucose.

The foregoing exposition of the manner of determining the insulin dosage in a particular case is only one of the many methods which can be utilized. It is, however, the method of greatest simplicity and the one I have found most useful in the greatest number of cases.

V. *What Cases Shall Receive Insulin*—In the early days of insulin therapy, I was inclined to feel that only exceptional cases would need insulin. In l oking over my clinical material in the University of California Metabolic Division of the out-patient department, I found numerous cases that had apparently done well for several years on low caloric diets. However, as our experience with insulin has accumulated, it becomes clear that its use will be gradually wider and wider. Probably the largest group of cases that require insulin are those in which small doses daily, say from ten to twenty units, are sufficient. In consideration of this experience, I have now reversed my opinion and believe it is the exceptional case of diabetes that would not be better off with insulin than without it. I do not believe that many diabetics are so mild that they can constantly manage a properly balanced 2000 to 2500 calorie diet without showing urinary sugar, and if this is true, it would appear that most diabetics need insulin if they hope to lead anything like a normal life and maintain anything like a normal metabolism.

VI. *Overdosage With Insulin—The Hypoglycemic Reaction*—Overdosage with insulin produces a lowering of the blood-sugar to subnormal levels, and is accompanied by a fairly well-defined symptom-complex. The patient notices a general sense of weakness, trembling, drowsiness, and hunger which comes on usually from one to two hours after the administration of the insulin. Slight overdosage may occur at any time during the use of the drug, but it is not attended with serious results. If it recurs frequently, it is direct evidence that the dosage is too high or the diet insufficient.

This hypoglycemic reaction is promptly and readily overcome by the immediate administration of a glass of orange juice containing 10 to 15 grams of glucose or 20 grams of milk chocolate.

Patients who are to receive insulin are always instructed in this method of controlling this condition at the outset of treatment, and to the present time, I have not seen nor read of any serious accidents from overdosage.

VII. *Hospital Instruction and Home Treatment*—During the period of hospitalization, the patient is given systematic instructions in planning quantitative diets, in the use of insulin, with particular reference to dosage and the care and use of the hypodermic syringe, and in the performance of the Benedict's test for the presence of sugar in the urine.

By means of a special diet card the instructions in dietetics are greatly simplified and readily mastered.

The home management of patients, after the preliminary hospitalization, has been entirely satisfactory. The patient examines his urine each day; he plans and follows a carefully prepared dietetic regime of known food value, and he takes his insulin in the proper dosage as was determined for him in the hospital. The cases that I have followed under these conditions have been attended with pleasing and satisfactory results.

Frederick Allen is still of the opinion that slight undernutrition is the ideal state for the diabetic to maintain even with the use of insulin. I am of the same opinion, and accordingly I warn my patients to prevent overweight and adjust their final diets which they are to follow at home, with this in mind.

VIII. *Acidosis*—The problem of acidosis is a big one, and I hesitate to enter into its discussion. Its extreme importance, however, compels me to present briefly the general plan of management of this condition I have adopted since using insulin.

Clinically, acidosis is characterized by drowsiness, deep and rapid breathing, nausea, and often vomiting. The clinical picture is confirmed by certain laboratory findings, such as acetone bodies in the urine and a lowering of the carbon dioxide combining power of the blood plasma. All degrees of acidosis occur depending on the amount of acetone bodies in the blood and tissues; however, its presence in any degree must be regarded as a serious affair.

Impending acidosis requires the withdrawal of all food except the C represented in the juice of citrus fruits. A pint to a quart of orange juice should be given each twenty-four hours. Besides this other fluids should be forced, and between five and ten quarts of water should be taken in this period. Where oral administration of fluids is not possible, saline solution by rectum, or subcutaneously, should be utilized. An enema should be given at the start and repeated daily if necessary. The use of sodium bicarbonate still has a place in this condition. The amount to be used will vary in individual cases between 5 and 50 grams per twenty-four hours, by mouth or rectum.

Finally, the presence of acidosis, in any extent, indicates the prompt use of insulin. As a rule, thirty to forty units of insulin should be given intravenously and twenty to thirty units subcutaneously from the start. A blood sample is taken for the determination of the blood-sugar and the carbon dioxide combining power of the blood plasma. The urine is also followed closely for the presence of sugar and acetone bodies. Subsequent insulin injections should be made every hour or two hours, the dosage depending on the clinical condition of the patient and the laboratory findings. If the blood-sugar remains well above normal and sugar is still coming through in the urine, high dosage of insulin (thirty to forty units) is still required. The subsequent doses of insulin, however, should be accompanied by the administration of glucose, either dilute glucose syrup or orange juice with sugar, so that for each unit of insulin given, one gram of sugar is given. The purpose of the glucose is to safeguard against a severe hypoglycemic reaction as the blood-sugar falls, and further, to combat the acidosis itself. The more sugar given, the more that will be utilized with a fixed amount of insulin. The utilization of glucose is also essential for the combustion of the accumulated acetone bodies and glucose also has a desirable diuretic effect. If the patient can retain nothing by mouth, the glucose can be given in a 5 per cent saline solution by rectum, intravenously or intraperitoneally.

As acidosis decreases, the insulin dosage required is reduced and the intervals between doses lengthened. The food during this preliminary period is solely the C of the orange juice. Following the disappearance of the acidosis, the diet can be gradually increased to include some P, more C, and finally, a small amount of F. Subsequently, the diet and the insulin dosage can be balanced in the usual way.

This, in a general way, represents the method of treatment in acidosis. For patients first seen in deep coma, the above plan is followed except more intensively and with higher insulin dosage.

IX. *Conclusions* — Our experience leaves no doubt that the pancreatic extract, insulin, is a valuable therapeutic agent. This is measured objectively in terms of lowered blood-sugar values, decreased glycosuria, and in the control of ketosis, as well as in the relief of symptoms.

There is a striking variation in the extent of the response to therapy with insulin in individual cases. This is accounted for in several ways, complicating infections and difference in severity of the diabetes, appear to be the chief factors.

The effects of insulin can be quantitatively measured in a given case by a careful balancing of a measured diet against a measured dose of the drug. One method of obtaining the proper dosage of insulin is presented above, but no hard-and-fast rule of procedure should be followed blindly in all cases. One must study each case intelligently not only to determine the dosage required to enable the patient to ingest enough food to carry out the normal activities of life, but the division of doses and time relationship between meals needs to be worked out in order to avoid annoying and probably harmful periods of hypoglycemia.

We are only in the beginning of our knowledge concerning the therapeutic use of insulin and undoubtedly, as time passes and experience accumulates, much valuable information, which we now lack, will be forthcoming.

(1251 Flood Building.)

Community's Right to Enforce Physical Fitness—If ignorance and quackery on the part of those who undertake to treat my sick fellow-citizen endanger his health, and thus make him less capable, or incapable, of bearing those economic and military burdens that actually or potentially are his, then I as a member of the body politic, in order that his burdens may not be thrust on me, have the right to see that he is not exposed to ignorance or quackery. For I must pay taxes to support and care for my fellow-citizen, when he is disabled by disease, and I, therefore, am entitled to see that he does not recklessly or ignorantly endanger his health. The soundness of this principle is universally conceded in laws prohibiting bad food and impure drugs, unwholesome dwellings, and insanitary working conditions. No one clamors for the right of every citizen to buy bad food for himself and his family, to live in unwholesome quarters, and to work under insanitary conditions. With respect to these matters, the claim that each citizen's health is his own, to do with as he likes, seems to have no place. What basis is there, then, for the claim that he, when sick, has the right to retard, and it may be to prevent, his restoration to health, by employing incompetent practitioners? My interest in the health of my neighbor is not limited, however, by economic considerations. In case of war, riot or insurrection, I, in common with my able-bodied fellow-citizens, may be impressed into service to defend the common welfare, even at the risk of my life, and I am entitled, on that account, to see that my share in the burden and risk of defense is not increased by the fact that a fellow-citizen who should share them with me has unnecessarily incapacitated himself for such duty, either through the employment of dishonest or incompetent practitioners, or otherwise. Finally, I think I may justly claim the right to see that my fellow-citizen does not, through the employment of incompetent practitioners, expose me and my family to infection, or thrust upon the community an epidemic, in the cost of which I, as a taxpayer, may have to share. I, then, and through the Government and for the common weal, have a right to have incompetent practitioners barred, no matter how much my ignorant neighbor may be willing to endure or encourage them.—William C. Woodward, M. D., Federation Bulletin, September, 1923.

DEMONSTRATING THE TUBERCLE BACILLUS*

By ERNST A. VICTORS, M. D., San Francisco

The tubercle bacillus holds a rather unique position in bacteriology in that its identification, based upon morphologic characteristics alone, is usually sufficient for the diagnosis of a tuberculous process. A biologic diagnosis, owing usually to the time factor, is infrequently disregarded and is generally limited in its application to such specimens in which the organism has evaded microscopic detection. In fact, the diagnosis of tuberculosis must be viewed as presumptive, unless corroborated by positive laboratory findings.

This paper ventures no originality in technical procedure, but is rather a summary of the result of several years' experience in selecting published methods, with individual modifications, with a view to advancing laboratory efficiency and to minimize, without sacrifice of precision, the time of investigation. I think it is safe to assume that, with the commonest tuberculous involvements, pulmonary and renal, by the time the individual reaches a condition of ill health for which he consults a physician, the tuberculosis is "open." Tubercle bacilli are present continually or continuously in the exudate or secretion. This belief carries with it the importance of intensive investigation in suspected cases—re-examinations and protracted material collections, and lends comfort to an ultimate negative conclusion.

CONCENTRATION

Homogenization and fluidification of denser material—sputum, pus, feces, and tissues—preceding depositing for smear preparations is now a well-established laboratory procedure. Many methods are in use, each claiming its group of adherents. We have been inclined to discard methods involving the use of ligroin, chloroform and other immiscible fluids of unequal density for bacterial layering as having no advantage over simple liquefaction by weak sodium hydrate or chlorine solutions and reduction of density with distilled water or alcohol and rapid centrifugalization. Liquefaction by autolysis or pressure steam is not practicable.

One present technic of concentration is to add to the entire specimen submitted, generally in the container in which the specimen is received, a sufficient amount of Lorenz solution to render it semi-liquid, so that an average fraction can be obtained. Small specimens, less than 10 to 20 cm., are used entire. Tissue and curettings are first pulped with sand.

A portion of such partially homogenized specimen—about 15 cm.—is transferred to a heavy glass rubber stoppered bottle, 30 by 100 cm., having no neck. Lorenz solution is again added, in sufficient amount to immediately complete homogenization, aided by vigorous hand-shaking. The bottle is then partially filled with distilled water to reduce density, again agitated and a portion transferred to a 15 cm. centrifuge tube and rapidly spun for twenty minutes.

Lorenz solution is a substitute for Uhlenhuth's

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